UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,678	07/07/2003	Alexander D. Romaschin	1148-1-002 CIPF	7389

23565 7590 01/28/2004

KLAUBER & JACKSON
411 HACKENSACK AVENUE
HACKENSACK, NJ 07601

EXAMINER	
SHAHNAN SHAH, KHATOL S	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 01/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/614,678	ROMASCHIN ET AL.	
	Examiner	Art Unit	
	Khatol S Shahnan-Shah	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicants' response to pre-Exam formalities received October 29 2003 is acknowledged.

Corrected Oath or Declaration was filed.

2. Currently claims 1-20 are pending and are under consideration.

Information Disclosure Statement

3. Applicants' Information disclosure statement received July 7, 2003 is acknowledged.

The references have been considered by the Examiner. See attached PTO 1449.

Drawings

4. Formal drawings were received on July 7, 2003. These drawings are approved by the

Examiner.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1-20 are rejected under the judicially created doctrine of obviousness-type double

patenting as being unpatentable over claims of 1-16 and 24-31 of U.S. Patent No. 5,804,370.

Although the conflicting claims are not identical, they are not patentably distinct from each other

because both claims of the instant application and those of Pat No.U.S. Patent No. 5,804,370 are drawn to method for quantitating the level of preselected analyte present in a sample. While claims 1-16 and 24-31 of U.S. Patent No. 5,804,370 recite a method for detecting an analyte in a body fluid for determining the presence or extent of sepsis, it would have been obvious to one of ordinary skill in the art to use similar methods for determining the presence of analytes in body fluids, which is indicative of infection and sepsis.

This is an obviousness-type double patenting rejection.

7. Claims 1-20 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of 1- 11 of U.S. Patent No. 6,203,997.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both claims of the instant application and those of Pat No.U.S. Patent No. 6,203,997are drawn to method for quantitating the level of preselected analyte present in a sample. While claims 1- 11 of U.S. Patent No. 6,203,997 recite a method for detecting an analyte in a body fluid for determining the presence or extent of sepsis, it would have been obvious to one of ordinary skill in the art to use similar methods for determining the presence of analytes in body fluids, which is indicative of infection and sepsis.

This is an obviousness-type double patenting rejection

8. Claims 1-20 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of 1- 15 of U.S. Patent No. 6,306,614.
Although the conflicting claims are not identical, they are not patentably distinct from each other because both claims of the instant application and those of U.S. Patent No. 6,306,614 are

drawn to method for quantitating the level of preselected analyte present in a sample. While claims 1- 15 of U.S. Patent No. 6,306,614 recite a method for detecting an analyte in a body fluid for determining the presence or extent of sepsis, it would have been obvious to one of ordinary skill in the art to use similar methods for determining the presence of analytes in body fluids, which is indicative of infection and sepsis.

This is an obviousness-type double patenting rejection.

Claim Rejections - 35 U.S.C. § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

10. Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 4, 8, 10, 15 and 17 are rejected as being vague and indefinite for the recitation of "oxidant-producing phagocytic cells." What are these oxidant-producing phagocytic cells? This terminology is not known in the art.

Claims 7, 13 and 15 recite broad limitations such as "analyte is indicative of the extent of infection or sepsis." Is it bacterial infection or viral infection or parasitic infection? How many analytes are involved in each one of these infections and sepsis?

Claims 1, 8 and 15 recite the limitation "the amount". There is insufficient antecedent basis for this limitation in the claims.

Claims 1, 8 and 15 recite the limitation "the presence ". There is insufficient antecedent basis for this limitation in the claims.

Claims 8 and 15 are rejected as being vague and indefinite for the recitation of " that produced by a maximal amount of immunocomplexes." What constitute the maximal amount of immunocomplexes and how does some one know that amount?

Claims 6, 12 and 18 are indefinite in the recitation of the abbreviations "fMLP". Full terminology should be explained when the abbreviation appears in the claim for the first time.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-20 are rejected under 35 U.S.C. 102 (b) as being anticipated by over Romaschin et al. (WO 94/29728).

Claims are drawn to a method for detecting an analyte in a body fluid indicative of the extent of infection or sepsis comprising:

a. forming an immunocomplex between analyte and antibody;

b. reacting the immunocomplex with an oxidant producing phagocytic cell;

c. measuring the amount of oxidant produced as an indicator of the presence of absence of said analyte.

Romaschin et al. disclose a method for detecting an analyte in a body fluid indicative of the extent of infection or sepsis comprising:

a. forming an immunocomplex between analyte and antibody (see abstract, claims specially claim 1 and summary of invention pages 6-7);

b. reacting the immunocomplex with an oxidant producing phagocytic cell (see abstract, claims specially claims 1-4 and summary of invention pages 6-9);

c. measuring the amount of oxidant produced as an indicator of the presence of absence of said analyte. (see abstract, claims specially claims 1-7 and summary of invention pages 6-9).

Romaschin et al. disclose whole blood (see claim 2) and oxidant- producing cells such as neutrophils and monocytes (see page 7 and claims 3, 26, 27, and 52). Romaschin et al. also disclose different activators such as zymosan and opsonized zymosan and osponized latex particles (see pages 16-17). Romaschin et al. teach that the amount of oxidant produced is achieved using a chemiluminescent compound which reacts with said oxidant to generate light and further teach that chemiluminescent compound is selected from group consisting of luminol, lucigenin and pholasin (see pages 6-9 and claims). Romaschin et al. teach gram negative bacteria, gram positive bacteria, virus, fungi, gram negative endotoxin, inflammatory mediators such as tumor necrosis factor, interleukin 1, 6, 8, interferon and transforming growth factor ß (see pages 7, 11, 23 and example 1). They teach gram-negative bacterial infection such as E. coli (see examples 1-3, pages 23-25 and table 12). They teach monoclonal antibodies of IgM or IgG class and anti-lipopolysaccharide antibody (see pages 8, 15 and 23). Romaschin et al. teach both methods of diagnosis and monitoring the treatment of sepsis or infection in a human or animal

patient (see claim 25). They also teach a method wherein a control is provided (see claims 8, 28 and table 10).

The prior art teaches the claimed method.

Since the office does not have the facilities for examining and comparing applicants' method with the method of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed method and the method of the prior art (i. e., that the method of prior art does not possess the same method steps, material used and functional characteristics of the claimed method). See In re Best, 562 F.2 d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 1-20 are rejected under 35 U.S.C. 103 (a) as being unpatentable over De Baetselier (US Patent 4,737, 455) in view of Winkelhake et al. (Journal of Infectious diseases, Vol. 165, pp. 26-33, 1992).

Claims are drawn to a method for detecting an analyte in a body fluid indicative of the extent of infection or sepsis comprising:

a. forming an immunocomplex between analyte and antibody;

b. reacting the immunocomplex with white blood cell;

c. measuring the amount of oxidant produced as an indicator of the presence or absence of said analyte.

De Baetselier describes a method of analyzing biological fluids such as blood, serum, etc., comprising:

a. providing hybrid phagocyte cells;

b. treating the hybrid phagocyte cells with a fluid to be analyzed;

c. combining them with a stimulator and anti-stimulator antibodies;

d. measuring the analyte by chemiluminescence.

(see column 17 and claims specially claims 14-15).

De Baetselier teaches that the property of phagocyte cells to show chemiluminescence when activated by certain chemical or immunological agent is used for qualitative or quantitative measurement of analytes in biological fluids. A variety of analytes such as endotoxins, lymphokines, membrane specific antibodies and their antigens, toxic substances and others can be analyzed by this method (see abstract). A chemiluminescent substrate, such as luminol or lucigenin, is added to intensify the chemiluminescence (col. 7, line 3 – 18-21). The target analyte may be a stimulator such as micrococci, plasmodium, trypanosoma, streptococci, etc. De Baetselier explicitly uses hybrid phagocyte cells, instead of normal phagocyte cells, such as neutrophils, leukocytes and monocytes, to provide a "standardized" chemiluminescence response. Thus, De Baetselier differs in using hybrid phagocyte cells; and, in using a different control sample, i.e. one without the fluid to be analyzed rather than one without the antibodies against the target antigen. However, it would have been obvious to one of ordinary skill in the art to modify the method of De Baetselier by using the claimed normal phagocyte cells to avoid the trouble and expense associated with the procurement of special hybrid phagocyte cells; and, to modify the control sample by deleting reagent antibody instead of sample fluid so as to control

for the variability of the normal phagocyte cells in the sample fluid; and, to run a standard curve, e.g. using a "maximum" expected amount of analyte/antigen in obtaining said standard curve, for conventional quantitation of analyte. De Baetselier clearly teaches the amount of chemiluminescence produced is proportional to the amount of stimulator/analyte/antigen present. (See abstract; col. 1, lines 30-41; col. 7, line 3 – col. 8, line 33). De Baetselier does not teach gram negative bacteria such as *E.coli, Klebsiella pneumoniae* or *Pseudomonas aeruginosa* as analytes. However detection of gram negative bacteria for diagnosis of sepsis and infection using antigen-antibody interaction is well known the art and are routine in clinical diagnosis. Winkelhake et al. teach gram-negative bacteria such as *E.coli, Klebsiella pneumoniae* or *Pseudomonas aeruginosa* as analytes.

Conclusion

15. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (703) 308-8896. The examiner can normally be reached from7: 30 AM - 4 PM on Monday through Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned to is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

Art Unit

January 24, 2004

JAMES HOUSEL 1/26/04
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600